Memory Impairment in MS correlates to Hemodynamic Response in Event-related fMRI of Episodic Memory

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Introduction

An estimated 40-50% of MS patients have some cognitive deficit, with memory deficits included as a common manifestation of cognitive dysfunction [1]. In previous studies of healthy controls engaged in word recognition tasks, functional differentiation has been found between novel words and previously presented works [2]. Furthermore, one study investigated the correlation between the California Verbal Learning Test (CVLT) and functional activation differences. For novel words, CVLT performance showed a significant positive correlation with the right anterior hippocampus. For previously seen words, activation in the right dorsolateral prefrontal cortex was positively correlated with CVLT performance [3].

In addition to investigating simple recognition, researchers have also looked more closely at activation in the prefrontal cortex during different types of word recognition tasks [4]. In a recognition task using previously seen words (true), closely related new words (false), and unrelated new words (new), Cabeza and colleagues found a disassociation between the bilateral dorsolateral prefrontal cortex (DLPFC) and the left ventrolateral prefrontal cortex (VLPFC). While the DLPFC seemed to reflect monitoring of retrieved information, the VLPFC seemed to be active in semantic processing.

We hypothesize that brain regions involved in the performance of a word recognition task will have a hemodynamic response that is directly related to the degree of memory impairment in MS subjects. Specifically, we expect degree of activation word recognition brain regions will correlate with performance on the CVLT.

Methods

The following scans were performed on seventeen female and two male right-handed subjects with multiple sclerosis (mean age 44.84 (9.01); mean EDSS 2.47 (1.47)). Anatomic whole-brain T1-weighted inversion recovery turboflash (MPRAGE): 120 axial slices, thickness 1.2mm, Field-of-view (FOV) 256mm x 256mm, matrix=256 x 128. Resting state whole-brain EPI scan: 132 volumes of 31-4mm thick axial slices TE/TR/flip=29ms/2800ms/80, matrix=128 x128, 256mm x 256mm FOV, BW=250KHz. In addition, three whole-brain EPI scans were run while subjects engaged in each of two tasks: First, an incidental encoding task (WE), during which subjects were shown 60 words for 2000ms each asked to decide if each word was abstract or concrete. Subjects were told that they would be asked about the words later. After twenty minutes, two word retrieval (WR) scans were used to measure recognition memory for words seen in the WE scan [5]. All subjects were also administered the California Verbal Learning Test (CVLT), a test of verbal learning and memory [6].

Corrections include slice average covariate removal and physiologic noise correction using PESTICA [7] and RETROICOR [8], motion correction, a regression of the second order motion parameters of each voxel [9], and spatial filtering with a 2D hamming filter [10]. Finally, all timeseries were detrended and digitally filtered to remove fluctuations above 0.08Hz [11].

Analysis

The t-maps of the five highest performing subjects on the WR task were merged and used to select regions of interest for the correlation analysis. Regions of interest included areas in bilateral BA 47 and BA 9, and left BA 45, 44, 7, and 6. WR events were split into “encoded” and “non-encoded” words for each subject based on responses during the WR task. “Encoded” words were those that were correctly identified, while “non-encoded” words were those that were not identified as having been seen in the WE task. The correlation between the fit hemodynamic response amplitude during the WR task and CVLT score was calculated for all 19 subjects for both the encoded and non-encoded words.

Results

Areas that showed a significant correlation with the CVLT ($p<10^{-4}$) included BA 47 [-43 22 -3], on the ventral lateral portion of the inferior frontal gyrus, BA 45 [-49 22 21], on pars triangularis, BA 7 [-27 -63 45], the somatosensory association cortex, and BA 6 [-40 -1 48], the premotor cortex important for planning movement. Although the regions of interest were somewhat constricted by the subselection of regions based on activation, those areas that did show a correlation are closely aligned with activated areas (Fig. 1).

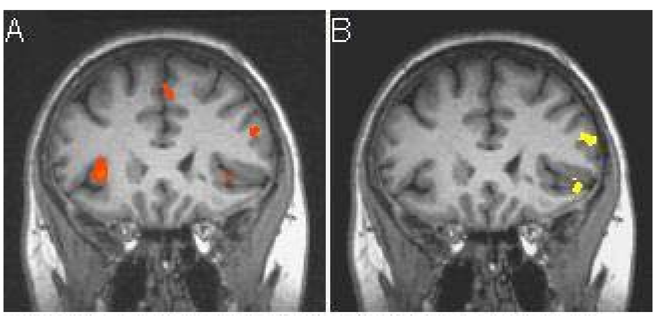

Fig. 1 A. Functional activation during WR suggested areas for B. correlation analysis of CVLT scores and hemodynamic response amplitude for encoded words, with BA 47 and 45 shown.

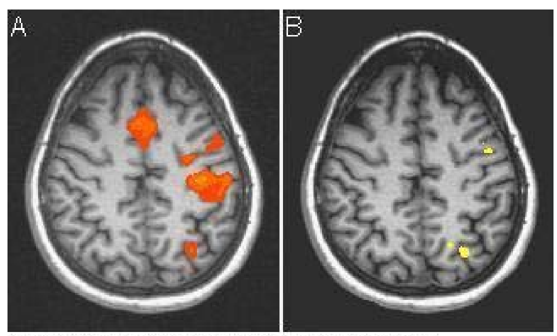

Fig. 2 A. Functional activation showing primary motor, supplementary motor, and premotor cortex, in addition to the somatosensory association area of the parietal cortex. B. Correlations in BA 6 and BA7.

Discussion/Conclusion

The region of BA 47 involved in the present research has been repeatedly implicated in semantic processing [12]. The CVLT, in particular, employs semantic clustering within the task [6]. Left VLPFC (BA 45) is theoretically involved in semantic processing as well. The premotor cortex is involved in planning movement. Subjects responded to the presentation of words with a button press, and subjects with more intact memory skills may have been better primed to react to the presentation of the word stimulus. MS patients exhibit significant positive correlations between cortical areas active during a word recognition task and performance on a test of verbal memory. Results suggest that the degree of activation produced during performance of the word recognition task may provide a potential marker of verbal memory performance in patients with MS.

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